UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,423	02/25/2004	Allen Wayne Mangel	PG3731US2	2803

23347 7590 06/29/2005

DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY
GLAXOSMITHKLINE
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,423	MANGEL ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2-25-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Preliminary Amendment filed February 25, 2004 is acknowledged. Claims 1-21 are canceled. New claims 22-25 are presented and represent all of the claims now under consideration. Updated priority information is noted.

An Information Disclosure Statement filed February 25, 2004 is further acknowledged and has been reviewed.

Claims 22-25 are rejected under 35 U.S.C. 112, both first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the invention, and for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

Applicants fail to particularly point out a definition of "a pharmaceutically acceptable derivative thereof" in claims 22-25. The metes and bounds of "derivative" cannot be precisely determined. Numerous compounds that lack enablement and an adequate teaching as to how to prepare them are encompassed in the claims. Undue experimentation would be required to embrace the scope of the claims. Applicants should recite those "derivatives" contemplated.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,759,413. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed compound in the patent is recited in instant claims 23 and 25. Claims 23 and 25 are drawn to treating non-ulcerative dyspepsia.

Claims 22-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 and 24 of U.S. Patent No. 6,831,097. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 19 and 24 recite the compound 2-(4-ethoxy-phenyl)-3,4-methanesulfonyl-phenyl)-pyrazolo[1,5-b]pyridazine for use in a method for treating a subject suffering from a condition which is mediated by selective inhibition of COX-2 and in a method of treating an inflammatory condition. This compound is recited in instant claims 23 and 25 for use in treating a condition that is mediated by selective inhibition of COX-2 and, in some instances, in a method of treating an inflammatory condition.

Claims 22 and 24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30 and 39 of U.S. Patent No. 6,780,870. Although the conflicting claims are not identical, they are not

patentably distinct from each other because claims 30 and 39 are directed to treating a human subject suffering from a condition that is mediated by COX-2.

Claims 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to the treatment of any non-ulcerative dyspeptic condition. Non-ulcerative dyspepsia broadly encompasses the inability to digest or a difficulty in properly digesting food in the alimentary tract and the abdominal discomfort or illness that results from this inability or discomfort. Various motility disturbances, as well as reflux disease, are non-ulcerative dyspeptic conditions.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation.

These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of any non-ulcerative dyspeptic condition comprising administering various compounds of unrelated structure that are characterized as COX-2 inhibitors.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the field of gastroenterology.

Each particular non-ulcerative dyspeptic condition has its own specific characteristics and etiology. The broad recitation "treatment of a mammal suffering from NUD comprising administering an effective amount of a COX-2 inhibitor" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any disease or disorder of the gastrointestinal tract that is characterized by indigestion.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of celecoxib or 8-acetyl-3-(4-methanesulfonyl-phenyl)-imidazol[1,2-a]pyridine for prokinesis; for lowering esophageal sphincter pressure following the administration of celecoxib; and for treating post-operative ileus following the administration of 2-(4-ethoxy-phenyl)-3,4-methanesulfonyl-phenyl)-pyrazolo[1,5-b]pyridazine.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular COX-2 inhibitor would be preferred for treatment of the many pathologies of the gastrointestinal tract that are associated with non-ulcerative dyspepsia. The skilled artisan would expect the interaction of a particular drug in the treatment of a particular non-ulcerative dyspeptic condition to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding or any criteria for extrapolating beyond the administration of celecoxib for prokinesis or for lowering esophageal sphincter pressure and for treating post-operative ileus following the administration of 2-(4-ethoxy-phenyl)-3,4-methanesulfonyl-phenyl)-pyrazolo[1,5-b]pyridazine. No direction is provided to treat any other conditions. Absent reasonable *a priori* expectations of success for using a particular COX-2 inhibitor to treat any particular non-ulcerative dyspeptic condition, one skilled in the gastroenterology art would have to test extensively many inhibitors to discover which are effective. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue

experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 22 and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Morgan, G., European Journal of Gastroenterology and Hepatology.

Morgan teaches the administration of selective COX-2 inhibitors for reflux esophagitis. See page 399, column 1, lines 13-15, under Conclusions, and Table 1 on page 398.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan, G., European Journal of Gastroenterology and Hepatology.

Morgan teaches COX-2 is expressed in inflammatory bowel conditions and that selective COX-2 inhibitors may have therapeutic potential both against inflammatory conditions, such as reflux esophagitis, and for gastrointestinal motility disorders. See Table 1 on page 398, as well as the discussion under "Conclusions". Morgan fails to recite specific species of COX-2 inhibitors as required by instant claims 23 and 25.

However, Morgan states in the last paragraph on page 397, selective COX-2 inhibiting NSAIDs have potential in the treatment of gastroesophageal reflux disease and reflux esophagitis. Therefore, one skilled in the gastroenterology art, in view of Morgan's teachings, would have been motivated to administer a known COX-2 inhibitor to treat a non-ulcerative dyspeptic condition. Such would have been obvious because a non-ulcerative dyspeptic condition may or may not be accompanied by inflammation. Morgan establishes the therapeutic benefit demonstrated when selective COX-2 inhibitors are administered in response to the expression of inducible COX-2 in various gastrointestinal pathological conditions characterized by dyspepsia.

Nó claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached Mondays to Fridays from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at telephone number 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

June 25, 2005